

REMARKS

Claims 4 and 6 have been amended to be written as independent claims. Claim 6 has further been amended to incorporate the language of claim 7, now cancelled. It is believed that none of these amendments constitute new matter, and their entry is therefore requested.

The Examiner restricted the claims of the invention between four Groups. Of these, Group II was directed to claims 4 and 5, and Group III was directed to claims 6-11 and 14-17. Group III was said not to be limited to the special technical feature. Claim 6 of Group III has been amended to be limited to the special technical feature of claim 4 of Group II.

It is believed that claims 4-6 and 8-11 have unity of invention and properly belong in a single group. That is, these claims relate to a product (claim 4), a process specifically adapted for the manufacture of the product (claim 5) and a use of the product (claims 6 and 8-11). 37 CFR §1.475(b)(3). Thus, Applicants propose that Group II be reformulated in accordance with 37 CFR §1.475 (b)(3) to include claims 4-6 and 8-11. Applicants elect this reformulated Group, i.e., claims 4-6 and 8-11, for examination.

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Serial No.: 09/462,931
19 April 2001
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MARKED-UP COPY OF THE AMENDED CLAIMS

4. (Thrice Amended) A monoclonal antibody or recombinant antibody fragment having the capability of binding [the] a human gamma-carboxylated osteocalcin fragment [according to claim 1], comprising the amino acid sequence

6 7

Tyr-Leu-Tyr-Gln-Trp-Leu-Gly-Ala-Pro-Val-Pro-Tyr-Pro-Asp-Pro-Leu-
17 21 24 30
Glu-Pro-Arg-Arg-Glu-Val-Cys-Glu-Leu-Asn-Pro-Asp-Cys-Asp-Glu-Leu-
Ala-Asp-His-Ile-Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-
Val (SEQ ID NO:2)

in which at least one of the glutamic acids in positions 17, 21 and 24 is gamma-carboxylated, characterized by the specificity to epitopes that have been identified on the gamma-carboxylated fragment of osteocalcin, wherein said fragment spans either

- i) from the amino acid in position 7 to the amino acid in position 30, or
- ii) from the amino acid in position 6 to the amino acid in position 30 of the amino acid sequence [described in claim 1] of SEQ ID NO:2, and that all three glutamic acids in the positions 17, 21 and 24 of said sequence are gamma-carboxylated.

6. (Amended) A non-competitive immunoassay for quantitative determination of a gamma-carboxylated osteocalcin fragment [according to claim 1] comprising the amino acid sequence

6 7

Tyr-Leu-Tyr-Gln-Trp-Leu-Gly-Ala-Pro-Val-Pro-Tyr-Pro-Asp-Pro-Leu-
17 21 24 30
Glu-Pro-Arg-Arg-Glu-Val-Cys-Glu-Leu-Asn-Pro-Asp-Cys-Asp-Glu-Leu-
Ala-Asp-His-Ile-Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-
Val (SEQ ID NO:2)

in which at least one of the glutamic acids in positions 17, 21 and 24 is gamma-carboxylated,
characterized in that a sample containing said fragment is exposed to two monoclonal antibodies or
recombinant antibody fragments which bind said gamma-carboxylated osteocalcin fragment, said
monoclonal antibodies or recombinant antibody fragments are specific to epitopes that have been
identified on the gamma-carboxylated fragment of osteocalcin, wherein said fragment spans either

- i) from the amino acid in position 7 to the amino acid in position 30, or
- ii) from the amino acid in position 6 to the mino acid in position 30 of the amino acid
sequence of SEQ ID NO:2, and that all three glutamic acids in the positions 17, 21 and 24 of said
sequence are gamma-carboxylated.